IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

RAVGEN, INC., **Plaintiff,** **v.** **QUEST DIAGNOSTICS INC.,** **Defendants.**	**CIVIL ACTION NO. 6:20-CV-00972-ADA** **JURY TRIAL DEMANDED**

PLAINTIFF RAVGEN, INC.'S OPENING CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

Pages

TABLE OF AUTHORITIES

Cases **Page(s)**

Statutes

Rules

TABLE OF EXHIBITS

Exhibit	Description
1	U.S. Patent 7,332,277 (the "'277 Patent")
2	U.S. Patent 7,727,720 (the "'720 Patent")
3	'277 Patent File History, July 14, 2006 Amendment in Response to Non-Final Office Action (RAVGEN-00012638–2687)
4	'277 Patent File History, May 30, 2007 Amendment in Response to Non-Final Office Action (RAVGEN-00012992–3058)
5	'720 Patent File History, December 17, 2007 Amendment in Response to Non-Final Office Action (RAVGEN-00015524–5546)
6	Excerpt of Defendant Quest Diagnostics Incorporated's Proposed Claim Construction, served on July 6, 2021
7	Defendant Quest Diagnostics Incorporated's Preliminary Invalidity Contentions, served on June 25, 2021
8	Defendant LabCorp's Proposed Claim Construction in *Ravgen, Inc. v. Laboratory Corporation of America Holdings*, Civ No. 6:20-cv-00969-ADA (W.D. Tex.), served on July 7, 2021
9	Defendants Natera, Inc. and NSTX, Inc.'s Proposed Claim Term Constructions in *Ravgen, Inc. v. Natera, Inc.*, Civ. No. 1:20-cv-00692-ADA (W.D. Tex.), served on November 25, 2020
10	Defendant's Proposed Claim Constructions in *Ravgen, Inc. v. PerkinElmer, Inc.*, Civ. No. 6:20-cv-00822-ADA (W.D. Tex.), served on November 16, 2020

INTRODUCTION

This patent infringement action involves technology for the preparation and/or analysis of "free" nucleic acids, including in non-invasive prenatal testing. Plaintiff Ravgen, Inc. ("Ravgen") owns fundamental patents relating to that technology, including U.S. Patent Nos. 7,332,277 ("the '277 Patent") and 7,727,720 ("the '720 Patent") (collectively, the "Patents-in-Suit"). Quest Diagnostics Inc. ("Quest" or "Defendant") commercializes genetic tests using free fetal DNA that include the patented methods. As discussed below, Ravgen proposes that the disputed claim terms be given their plain and ordinary meaning in the art, as supported by the intrinsic record. Quest's proposals, on the other hand, conflict with this Court's prior determinations regarding the same claim terms and its own positions taken in other proceedings. The Court should reject Quest's arguments and construe the claim terms according to their plain and ordinary meanings.

BACKGROUND

Ravgen incorporates by reference the background section from *Ravgen, Inc. v. Natera, Inc.*, Civ. No. 1:20-cv-00692-ADA, Dkt. 46 at 1-3 (W.D. Tex. Dec. 15, 2020) ("*Natera* case") and *Ravgen, Inc. v. PerkinElmer, Inc.*, Civ. No. 1:20-cv-00822-ADA, Dkt. 50 at 1-3 (W.D. Tex. Dec. 4, 2020 ("*PerkinElmer* case").

DISPUTED TERMS

I. "agent that [inhibits lysis of cells/impedes cell lysis][1] . . . wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor" ('277 Patent, Claims 55, 81; '720 Patent, Claim 1)

Ravgen's Proposed Construction	Quest's Proposed Construction
Plain and ordinary meaning	Indefinite.

[1] The phrases "inhibits lysis of cells," and "impedes cell lysis" are used synonymously in the claims and the intrinsic record, and Quest has confirmed that no dispute exists based on purported differences between those phrases. Therefore, "impedes"/"inhibits" and "cell lysis"/"lysis of cells" are used interchangeably herein, and "agent limitation" is used herein to refer to all versions of this claim term.

	If not indefinite, then means plus function pursuant to 35 U.S.C. § 112, sixth paragraph.[2]

The Court has already correctly construed the agent limitation according to its plain and ordinary meaning, and Quest provides no reason that would justify departing from the Court's prior analysis and determination that the agent limitation is not indefinite. Indeed, in construing the agent limitation in the prior litigations, the Court rejected the very arguments Quest plans to proffer that the agent limitation is indefinite. Further, both of Quest's litigation theories regarding the agent limitation—that the limitation is indefinite and that, in the alternative, it is subject to § 112 ¶ 6—are inconsistent with the positions Quest has taken in other proceedings. For example, Quest has filed three *inter partes* review petitions challenging the Patents-in-Suit with accompanying expert declarations that each apply the ordinary meaning of the agent limitation without identifying that limitation as subject to § 112 ¶ 6. Thus, the Court should reject Quest's arguments and adopt its prior construction of the agent limitation as plain and ordinary meaning.

A. No Basis Exists To Depart From The Court's Prior Determination That The Agent Limitation Is Not Indefinite.

In *Markman* proceedings involving the same Patents-in-Suit earlier this year, this Court correctly determined that the agent limitation is not indefinite and construed it according to its plain and ordinary meaning. *See Natera* case, Dkt. 88 at 2, Dkt. 93-1 at 2[3]; *PerkinElmer* case, Dkt. 78 at 2. In so doing, the Court rejected the same arguments Quest now seeks to relitigate in this case. The Court should reject those recycled arguments and once again construe the agent limitation according to its plain and ordinary meaning.

[2] Quest's proposed structure is set forth in Quest's Proposed Construction, attached hereto as Ex. 6. Ex. 6 at 2-7.

[3] The parties in the *Natera* case recently filed a Joint Motion To Enter Amended Claim Construction Order, proposing changes to the Court's original to reflect their understanding of the Court's intended rulings.

When the parties met and conferred regarding claim construction, Quest admitted that it plans to proffer the same arguments put forth by Defendants in the *Natera* and *PerkinElmer* cases, and directed Ravgen to its Preliminary Invalidity Contentions. Indeed, both of the bases set forth in Quest's Preliminary Invalidity Contentions for its assertion that the agent limitation is indefinite were previously addressed and rejected by this Court in those cases. Ex. 7 at 70-71.

First, Quest asserts that the agent limitation is indefinite based on its incorrect reading of the limitation—that the Markush group species "cell lysis inhibitor" is coextensive with the requirement that the claimed agent "inhibits cell lysis." *Id.* at 71 ("'Cell lysis inhibitor' is listed as a species within the recited Markush group of 'an agent that inhibits cell lysis' but it is unclear how it can be a species, or what the metes and bounds of the species are, because the term is a recitation of the entire Markush group."). That argument is identical to the arguments set forth by Defendants in the prior cases and correctly rejected by this Court. *See, e.g., Natera* case, Dkt. 88 at 2, Dkt. 93-1 at 2 (construing the "agent" limitation as plain and ordinary meaning); *Natera* case, Dkt. 49 at 11 (alleging that "cell lysis inhibitor" "circularly parrots that which it is trying to define by example"); *see also Natera* case, Dkt. 63 at 1, 5.

Second, Quest asserts that the agent limitation is indefinite because "the specification does not describe whether any particular concentration or amount of cell lysis inhibition [or membrane stabilization] is required to qualify as an 'agent that impedes [or inhibits] cell lysis, if cells are present.'" Ex. 7 at 71. That argument too was briefed and rejected during the prior *Markman* proceedings. *See PerkinElmer* case , Dkt. 78 at 2 (construing the "agent" limitation as plain and ordinary meaning); *PerkinElmer* case, Dkt. 55 at 13-17 (alleging that the "agent" term is indefinite because "[t]he specification provides no limits on these terms beyond their overlapping functions"); *see also PerkinElmer* case, Dkt. 63 at 5. Because Quest's arguments provide no new

support for its contention that the agent limitation is indefinite, the Court should decline to depart from its original determination that the agent limitation is **not** indefinite. *See, e.g., Personalized Media Commc'ns, LLC v. TLC Corp.*, Civ No. 2:17-cv-00433-JRG, 2018 WL 3207436, at *7 (E.D. Tex. June 29, 2018) (rejecting Defendants' indefiniteness argument by finding Defendants failed to "justif[y] departing from the Court's [previous] analysis and construction" that the term at issue to be definite).

Additionally, Quest has filed three *inter partes* review petitions challenging the Patents-in-Suit with accompanying expert declarations, in which Quest and its expert applied the ordinary meaning of the agent limitation in analyzing the claims. *See Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00791, Paper 003 at 24-25 (PTAB April 15, 2021) (declining to construe any terms, including those of the agent limitation), *Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00791, Ex. 1002 ¶ 31 (PTAB April 15, 2021) (same), *Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00790, Paper 001 at 39 (PTAB April 19, 2021) (same), *Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00790, Ex. 1202 ¶ 102 (PTAB April 19, 2021) (same), *Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00788, Paper 004 at 24 (PTAB April 16, 2021) (same), *Quest Diagnostics Inc. v. Ravgen, Inc.*, IPR2021-00788, Ex. 1002 ¶ 119 (PTAB April 16, 2021) (same). Those petitions and declarations demonstrate that Quest and its expert understand the scope of the agent limitation, further evidencing that the limitation is not indefinite. *Canon, Inc. v. TCL Elecs. Holdings Ltd.*, Civ. No. 2:18-cv-00546-JRG, 2020 WL 2098197, at *39 (E.D. Tex. May 1, 2020) (rejecting Defendants' indefiniteness argument and noting that the Petitioner of an IPR with whom Defendants was privy "was able to propose a construction on the [disputed term] for the petition for IPR"); *Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1380 (Fed. Cir. 2017) (reversing a finding of indefiniteness and noting that "[a]ppellees' other actions during litigation

also reflect that they understood [the term]"); *Ramot at Tel Aviv Univ. Ltd. v. Cisco Systs. Inc.*, Civ. No. 2:19-cv-00225-JRG, 2020 WL 2517581, at *12 (E.D. Tex. May 15, 2020) (declining to construe a term and noting that Defendant's proposed construction conflicts with its position before the PTAB that "'plain and ordinary' meaning [is] the proper construction").

Therefore, and for the reasons provided in the *Natera* and *PerkinElmer* cases, the Court should reject Quest's argument that the agent limitation is indefinite and construe that limitation according to its plain and ordinary meaning.

B. The Agent Limitation Is Not Subject To 35 U.S.C. § 112 ¶ 6.

The Court should also reject Quest's alternative theory that the agent limitation is subject to § 112 ¶ 6, and adopt its prior construction of the agent limitation as plain and ordinary meaning. Of the four sets of Defendants who have proposed constructions for the agent limitation, only Quest has asserted that the agent limitation may be subject to § 112 ¶ 6. *See, e.g.,* Ex. 8 at 2; Ex. 9 at 2; Ex. 10 at 2. And Quest itself and its own expert have applied the ordinary, non-means-plus-function meaning of the agent limitation in other proceedings, including in the three *inter partes* review proceedings challenging the Patents-in-Suit that analyze that limitation. Under applicable Patent Office regulations, "[w]here the claim to be construed contains a means-plus function or step-plus-function limitation as permitted under 35 U.S.C. § 112(6)" (37 C.F.R. § 42.104(b)(3)), Quest was required to "identify [in its petitions] the specific portions of the specification that describe the structure, material, or acts corresponding to each claimed function." *Id.* Yet none of those *inter partes* review petitions, which Quest filed earlier this year, identified the agent limitation as means plus function pursuant to § 112 ¶ 6. Nor did Quest's expert in those IPRs analyze the agent limitation as requiring any particular structures from the specification, let alone those Quest now identifies pursuant to § 112 ¶ 6. Based on those conflicting positions alone, the Court should reject Quest's litigation-inspired alternative theory that § 112 ¶ 6 applies to the agent

limitation in this case. *See Intellectual Ventures II LLC v. BITCO General Ins. Corp.*, Civ. No. 6:15-cv-00059, 2016 WL 125594, at *12-14 (E.D. Tex. Jan. 11, 2016) (finding a disputed term as not means-plus function and noting that "in the IPR petitions, Defendants did not allege that the term is a means-plus-function term"); *Blitzsafe Texas, LLC v. Honda Motor Co.*, Civ. No. 2:15-cv-01274-JRG-RSP, 2016 WL 4762083, at *12-14 (E.D. Tex. Sept. 13, 2016) (same).

Moreover, because Quest cannot demonstrate that the agent limitation recites function without reciting sufficient structure for performing that function, it cannot overcome the presumption that the agent limitation ***not*** be construed as means plus function subject to § 112 ¶ 6. Because the agent limitation does not include the word "means," it is presumptively not construed as a means-plus-function term. *Williamson v. Citrix Online, LLC*, 792 F.3d 1339, 1348 (Fed. Cir. 2015). To overcome that presumption, Quest must demonstrate that the claim term fails to recite sufficiently definite structure or else recites function without reciting sufficient structure for performing that function. *See id.* at 1349. "The correct inquiry, when 'means' is absent from a limitation, is whether the limitation, read in light of the remaining claim language, specification, prosecution history, and relevant extrinsic evidence, has sufficiently definite structure to a person of ordinary skill in the art." *realZoom LLC v. L Brands, Inc.*, No. 2:17-cv-00118-RWS, 2018 WL 2287613, at *13 (E.D. Tex. May 18, 2018); *see Zeroclick, LLC v. Apple Inc.*, 891 F.3d 1003, 1007 (Fed. Cir. 2018). Quest cannot make that showing in light of the claim language and the record.

Quest asserts that the term "agent" is a nonce word and that the recited "function" is "[an agent] that impedes cell lysis, if cell are present, wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor." Ex. 6 at 2. That theory lacks merit. First, the claim language, the specification, and the extrinsic record confirm that, in the context of the claims, "agent" is not a nonce word, but rather refers to a particular class of

structures that can be used to accomplish the claimed function ("imped[ing] cell lysis, if cell are present"): chemical substances that, when added to a biological sample containing cell free nucleic acid, impede lysis of any cells present in the sample. Second, the record confirms that the language of the agent limitation itself further restricts the structures for performing the claimed function to three well-defined categories of chemical substances that were known in the art at the time of the invention: "membrane stabilizer, cross-linker, and cell lysis inhibitor." Thus, in the context of the claims and in light of the intrinsic and extrinsic record, the agent limitation recites sufficiently definite structure to a person of ordinary skill in the art and therefore is not governed by § 112 ¶ 6.

In the context of the claims, "agent" is not a nonce word. As explained by Dr. Brian Van Ness, a professor of genetics and cell biology with decades of experience working in a lab with biological samples, in the field of the claimed invention, "agent" means a chemical substance capable of producing an effect. Van Ness Decl.[4] ¶¶ 32-33.[5] In the context of the claims, and as confirmed by the specifications, "agent" refers to particular chemical substances that, when added to a biological sample containing cell free nucleic acid, inhibit lysis of any cells present in the sample. *Id.* ¶¶ 34-46. Thus, the claimed function itself restricts the chemical structures that can meet the agent limitation. *See Allergan Sales, LLC v. Teva Pharms. USA, Inc.*, No. 2:15-cv-01471-JRG, 2017 WL 2968588, at *6 (E.D. Tex. July 12, 2017) (holding that the term "gelling agent" was not subject to § 112 ¶ 6 and should be construed as plain and ordinary meaning because "[t]he

[4] "Van Ness Decl." refers to the July 21, 2020 Declaration of Brian G. Van Ness, Ph.D., filed herewith.

[5] That understanding is consistent with the extrinsic evidence identified by Quest in support of its constructions. Van Ness Decl. ¶¶ 67-68 , Ex. E at 4225 (defining "agent" as being "capable of producing a physical, chemical, or biological effect"), Ex. F at 4248 (defining "agent" as "something capable of producing an effect" and illustrating this definition with a list of chemical substances).

term 'gelling agent' itself at least confines the claims to a particular function, and the function restricts the type of substance that can meet the gelling agent limitation.").[6]

Moreover, the agent limitation itself further confines the covered structures to three well-defined categories of chemical substances that were known in the art at the time of the invention: "membrane stabilizer, cross-linker, and cell lysis inhibitor." Van Ness Decl. ¶¶ 47-59. Quest's proposed construction mischaracterizes the agent limitation by including the entirety of that limitation, including those well-defined categories of structures, as the "recited function." But the claim language makes clear that the agent limitation does not encompass every conceivable way or means to perform the function of inhibiting cell lysis; rather, it provides particular classes of chemical structures that perform that function: membrane stabilizers, cross-linkers, and cell lysis inhibitors. *See Multilift Wellbore Tech., Ltd. v. ESP Completion Techs., LLC*, No. CV H-17-2611, 2018 WL 925062, at *13 (S.D. Tex. Feb. 16, 2018) (quoting *Skky, Inc. v. MindGeek, s.a.r.l.*, 859 F.3d 1014, 1019 (Fed. Cir. 2017)) (holding that the term "flow diverter" was not subject to § 112 ¶ 6 where the record indicated that that term "covers a broad class of mechanical structures that perform the function of diverting flow, but it does not disclose 'every conceivable way or means to perform the function.'").

For example, the specifications describe, and a person of skill in the art ("POSITA") at the time of the invention would have known, that numerous processes involved in sample collection

[6] Indeed several courts have construed the term "agent" in patents relating to biology without invoking § 112 ¶ 6. *Unimed Pharms., LLC v. Perrigo Co.*, Civ. No. 13-236-RGA, 2015 WL 1094601, at *4 (D. Del. Mar. 11, 2015) (construing "gelling agent" to mean "an agent capable of gelling"—*i.e.*, no means-plus-function treatment); *Depmed, Inc. v. Actavis Elizabeth LLC*, Civ. Nos. 12-1358 JAP, 12-2813 JAP, 2014 WL 316702, at *11 (D.N.J. Jan. 28, 2014) (determining that "gas generating agent" did not require construction and its plain and ordinary meaning applies—*i.e.*, no means-plus-function treatment); *Cadence Pharms., Inc. v. Paddock Lab'ys Inc.*, 886 F. Supp. 2d 445, 456 (D. Del. 2012) (construing "buffering agent" to mean "[a]n agent that helps the formulation resist change in pH"—*i.e.*, no means-plus-function treatment).

and preparation may cause stress that results in cell lysis, including drawing blood, storage, transport, blood clotting, and centrifugation. *See, e.g.,* '277 Patent at 32:40-53, 89:32-34, 220:40-44; Van Ness Decl. ¶¶ 60-62. And the specifications and claims disclose numerous methods for inhibiting cell lysis by preventing those stressors: for example, modifying the blood drawing technique, including by using particular types of needles, modifying the centrifugation protocols, and using plasma, in which clotting has been prevented, instead of serum. *See, e.g., id.*; '277 Patent at 16:37-38, 32:40-53, 89:11-13, 89:32-34, 220:40-44, Claims 13, 62, 88, 95, 96, 123, 130, 137; '720 Patent, Claims 22, 34. However, the agent limitation does not encompass all of those potential ways of inhibiting cell lysis, but rather requires the use of the particular structure recited: a chemical substance that is a membrane stabilizer, cross-linker, and/or cell lysis inhibitor. *See, e.g.,* Van Ness Decl. ¶¶ 47-59, 60, 63-64; '277 Patent at 31:57-32:21, 32:54–56, 226:27-230:21; '720 Patent at 31:43-54, 33:12-28, 33:60-62, 216:15-218:55. Thus, as in *Multilift Wellbore,* because the agent limitation of the asserted claims does not encompass all of the possible ways of inhibiting cell lysis, that limitation is not equivalent to ***any means*** for impeding cell lysis, if cell are present and therefore is not subject to § 112 ¶ 6. 2018 WL 925062, at *13.

To the extent that Quest contends that the breadth or functional language in the names of the recited chemical substances (membrane stabilizer, cross-linker, and cell lysis inhibitor) renders them purely functional and thus subject to § 112 ¶ 6, it is wrong as a matter of law. To the contrary, "[t]o determine whether a claim recites sufficient structure, it is sufficient if the claim term is used in common parlance or by persons of skill in the art to designate structure, even if the term covers a broad class of structures and even if the term identifies the structures by their function." *Skky, Inc. v. MindGeek, s.a.r.l.*, 859 F.3d 1014, 1019 (Fed. Cir. 2017) (internal quotation marks omitted); *Greenberg v. Ethicon Endo-Surgery, Inc.*, 91 F.3d 1580, 1583 (Fed. Cir. 1996) ("the fact that a

particular mechanism—here 'detent mechanism'—is defined in functional terms is not sufficient to convert a claim element containing that term into a 'means for performing a specified function' within the meaning of section 112(6). Many devices take their names from the functions they perform. The examples are innumerable, such as 'filter,' 'brake,' 'clamp,' 'screwdriver,' or 'lock.'"). For example, in *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, the court found that § 112 ¶ 6 did not apply to the term "an inhibitor of phosphodiesterase (PDE) V" even though PDE V inhibitors constituted a "diverse collection of different chemical structures," and "that class is not a small one" because such inhibitors were well known in the art at the time. Civ. No. 2:15-cv-1202-WCB, 2016 WL 6138124, at *8-11 (E.D. Tex. Oct. 21, 2016). Similarly, in *Allergan*, the court held that the term "gelling agent" was not subject to § 112 ¶ 6 not only because the recited function restricted the type of substance that could meet the gelling agent limitation, but even "[m]ore important[ly], the 'gelling agent' is not the point of alleged novelty, nor is the combination of the gelling agent with the other film composition ingredients." 2017 WL 2968588, at *6-7.

Here, the agent limitation is confined not only by the particular function recited—that it inhibits cell lysis, if cells are present—but also by the three well-defined categories of structures that must be used to inhibit cell lysis in the claims. Further, as in *Allergan* and *Erfindergemeinschaft,* the intrinsic record here demonstrates that it is the novel use of the claimed agent according to the claimed methods, rather than the agents themselves, that renders those methods patentable advances over the prior art. For example, during prosecution, the patentee explained that although prior art disclosed the use of such agents for "the ***preservation of intact fetal cells***," that disclosure "in no way would have suggested to one of ordinary skill in the art that the addition of an agent that inhibits cell lysis to samples would have provided any advantage in methods of ***isolating free fetal DNA***." Ex. 3 at -00012671; *see also* Ex. 4 at -00013025–29; Ex. 5

at -00015534–38; Van Ness Dec ¶ 58. Thus, as in *Allergan* and *Erfindergemeinschaft,* because the agent limitation here is confined to particular classes of structures that were known in the art at the time of the invention in other context, that limitation is not subject to § 112 ¶ 6. 2017 WL 2968588, at *6-7; 2016 WL 6138124, at *11.

Accordingly, Quest has not met its burden to overcome the presumption that the agent limitation is ***not*** a means plus function element governed by § 112 ¶ 6, and the Court should construe that limitation according to its plain and ordinary meaning.

II. "[a] method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid . . . and (b) detecting the presence of absence of the free nucleic acid." ('720 Patent, Claim 1)

Ravgen's Proposed Construction	Quest's Proposed Construction
Plain and ordinary meaning	Indefinite

The isolating and detecting limitations, at least as read in light of the '720 Patent specification, would inform a POSITA about the scope of the limitation with reasonable certainty. Indeed, in Quest's *inter partes* review petition challenging the '720 Patent and accompanying declaration, Quest and its expert understood and applied these limitations according to their ordinary meanings, further evidencing that they are not indefinite. *Quest Diagnostics, Inc. v. Ravgen, Inc.*, IPR2021-00791, Paper 003 at 24-25 (PTAB April 15, 2021) (declining to construe any terms of the '720 Patent), *Quest Diagnostics, Inc. v. Ravgen, Inc.*, IPR2021-00791, Ex. 1002 ¶ 31 (PTAB April 15, 2021) (same); *see Canon*, 2020 WL 2098197 at *39. Quest's attempts to render Claim 1 indefinite rely on improperly rewriting or simply ignoring the clam language. Accordingly, Quest cannot prove by clear and convincing evidence that the term is indefinite. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014).

A. Based On The Intrinsic Record, A POSITA Would Understand The Scope Of The Isolating And Detecting Limitations With Reasonable Certainty.

As explained by Dr. Van Ness, a POSITA would have readily understood the scope of the isolating and detecting limitations based on (1) the plain language of the claim alone or (2) the plain language of the claim in combination with the guidance provided by the '720 Patent specification.

First, a POSITA would understand the isolating and detecting limitations with reasonable certainty based on the plain language of the claim. Van Ness Decl. ¶ 72. Claim 1 recites a method for detecting ***a*** free nucleic acid. '720 Patent at Claim 1. The plain language makes clear that the method includes: (1) isolating free nucleic acid from a non-cellular fraction of a sample; and (2) detecting whether the particular free nucleic acid of interest is present or absent within the isolated free nucleic acid. *Id.* ¶ 74; '720 Patent at Claim 1. As Dr. Van Ness explains, a POSITA would understand that "isolating free nucleic acid" encompasses isolating a mixture of free nucleic acids. Van Ness Decl. ¶ 75. For example, if the sample is taken from a patient with a cancerous tumor, the isolated free nucleic acid may include: (1) the patient's normal cell free DNA and (2) circulating tumor DNA.[7] *Id.* ¶ 76. Dr. Van Ness further explains that a POSITA would understand that in the "method for detecting a free nucleic acid," "detecting the presence or absence of the free nucleic acid" may include detecting the presence or absence of a particular free nucleic acid of interest within the isolated free nucleic acid. *Id.* ¶ 77. For example, the method could include: (1) isolating nucleic acid from a non-cellular fraction of a sample of blood from a patient who was treated for a cancerous tumor; and (2) detecting whether circulating tumor DNA is present or

[7] The example of patient cell free DNA and circulating tumor DNA is for purposes of explanation only. Other forms of free nucleic acids, such as those described in the '720 Patent specification, also fall within the scope of Claim 1.

absent in the isolated nucleic acid (*e.g.*, to gauge whether tumor cells are present in the patient). *Id.* ¶ 78.

Second, a POSITA would understand the scope of the isolating and detecting limitations with reasonable certainty based on the plain language of the claim with the guidance provided by the '720 Patent specification. *Id.* ¶ 82. The specification provides a POSITA with information consistent with Dr. Van Ness's explanation described above. *Id.* ¶ 83. For example, the '720 Patent specification describes an embodiment providing "a method for detecting a nucleic acid molecule containing at least one mutation, wherein said method comprises: (a) isolating nucleic acid from a plasma sample . . . and (b) detecting the presence or absence of a nucleic acid molecule containing the mutation. In a preferred embodiment, the nucleic acid isolated is free nucleic acid." '720 Patent at 22:58-66. This embodiment, among others, describes detecting whether a particular nucleic acid—in this embodiment, a nucleic acid with a mutation—is present or absent within the isolated free nucleic acid. Van Ness Decl. ¶ 84. Further, a POSITA reading the '720 Patent specification would understand that the "method for detecting a free nucleic acid" includes "detecting the ***presence or absence*** of the free nucleic acid." For example, if the free nucleic acid of interest is circulating tumor DNA, detecting the ***presence*** of the tumor DNA "indicates the presence of the tumor cells [and] suggests that new or more aggressive treatments should be prescribed." '720 Patent at 296:46-48; Van Ness Decl. ¶ 85. Conversely, detecting the ***absence*** of the tumor DNA may suggest that the patient's current or past treatment is sufficient. *Id*.

Accordingly, a POSITA would understand the scope of the isolating and detecting limitations with reasonable certainty based on the plain language of the claim as well as the guidance provided by the '720 Patent specification.

B. Quest's Argument That The Isolating And Detecting Limitations Are Indefinite Lacks Merit.

Although the claim language, read in light of the intrinsic record, informs a POSITA of the scope of the isolating and detecting limitations with reasonable certainty, Quest argues that the limitations are indefinite. Specifically, Quest argues that the limitations are indefinite because: (1) "it is not possible to detect the absence of free nucleic acid after it has been isolated"; and (2) "it is not possible to detect free nucleic acid by detecting its absence." Ex. 7 at 73. Both of Quest's arguments are incorrect.

First, Quest's argument that "it is not possible to detect the absence of free nucleic acid after it has been isolated" is based on Quest improperly rewriting Claim 1 to read: "[a] method for detecting a free nucleic acid, wherein said method comprises: (a) isolating ***the*** free nucleic acid . . . and (b) detecting the presence or absence of the free nucleic acid." But that is not the claimed invention. Rather, the claim requires a "method for detecting ***a*** free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid . . . and (b) detecting the presence of absence of ***the*** free nucleic acid." As described above, that method includes isolating some free nucleic acid, and detecting whether the particular free nucleic acid of interest is present or absent in the isolated free nucleic acid. Van Ness Decl. ¶¶ 77-78, 84. Accordingly, Quest's argument fails.

Second, Quest's argument that "it is not possible to detect free nucleic acid by detecting its absence" fabricates confusion regarding the scope of Claim 1 where none exists based on the plain language. The claim language itself makes abundantly clear that "detecting a free nucleic acid" includes "detecting the presence or absence of the free nucleic acid." '720 Patent at Claim 1. Further, as Dr. Van Ness explained, a POSITA would understand that in the context of a diagnostic procedure, the plain and ordinary meaning of "detect" or "detecting" can mean detecting the presence or absence of a nucleic acid of interest. Van Ness Decl. ¶¶ 79-80, 85. By way of example,

the title of the '720 Patent, "Methods for Detection of Genetic Disorders" does not signify that embodiments described within can only be used to detect the presence of disorders. Instead, as the term is used by POSITAs, such methods can be also be used to detect the absence of disorders. *Id.* ¶ 79.

Accordingly, Quest's arguments should be rejected and the isolating and detecting limitations should be found not indefinite.

CONCLUSION

For the foregoing reasons, Ravgen respectfully requests that the Court construe the disputed claim terms as proposed by Ravgen.

Dated: July 21, 2021

By: /s/ *Kerri-Ann Limbeek* (*pro hac vice*)

Deron R. Dacus
State Bar No. 00790553
THE DACUS FIRM, P.C.
821 ESE Loop 323, Suite 430
Tyler, TX 75701
Phone: (903) 705-1117
Fax: (903) 581-2543
ddacus@dacusfirm.com

John M. Desmarais (*pro hac vice*)
Kerri-Ann Limbeek (*pro hac vice*)
Jamie L. Kringstein (*pro hac vice*)
Kyle G. Petrie *(pro hac vice*)
Joze Welsh (*pro hac vice*)
Jun Tong (*pro hac vice*)
Deborah J. Mariottini *(pro hac vice*)
Peter Zhu (*pro hac vice*)
DESMARAIS LLP
230 Park Avenue
New York, NY 10169
Telephone: 212-351-3400
Facsimile: 212-351-3401
jdesmarais@desmaraisllp.com
klimbeek@desmaraisllp.com
jkringstein@desmaraisllp.com
kpetrie@desmaraisllp.com
jwelsh@desmaraisllp.com
jtong@desmaraisllp.com
dmariottini@desmaraisllp.com
pzhu@desmaraisllp.com

Attorneys for Ravgen, Inc.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that all counsel of record who are deemed to have consented to electronic service are being served with a copy of this document via the Court's CM/ECF system on July 21, 2021.

Dated: July 21, 2021

/s/ *Kerri-Ann Limbeek*

Kerri-Ann Limbeek
E-mail: klimbeek@desmaraisllp.com
DESMARAIS LLP
230 Park Avenue
New York, NY 10169
Telephone: 212-351-3400
Facsimile: 212-351-3401